



The Role of Detection in Biodefense

2003 New England Bioterrorism Preparedness Workshop

10 June 2003

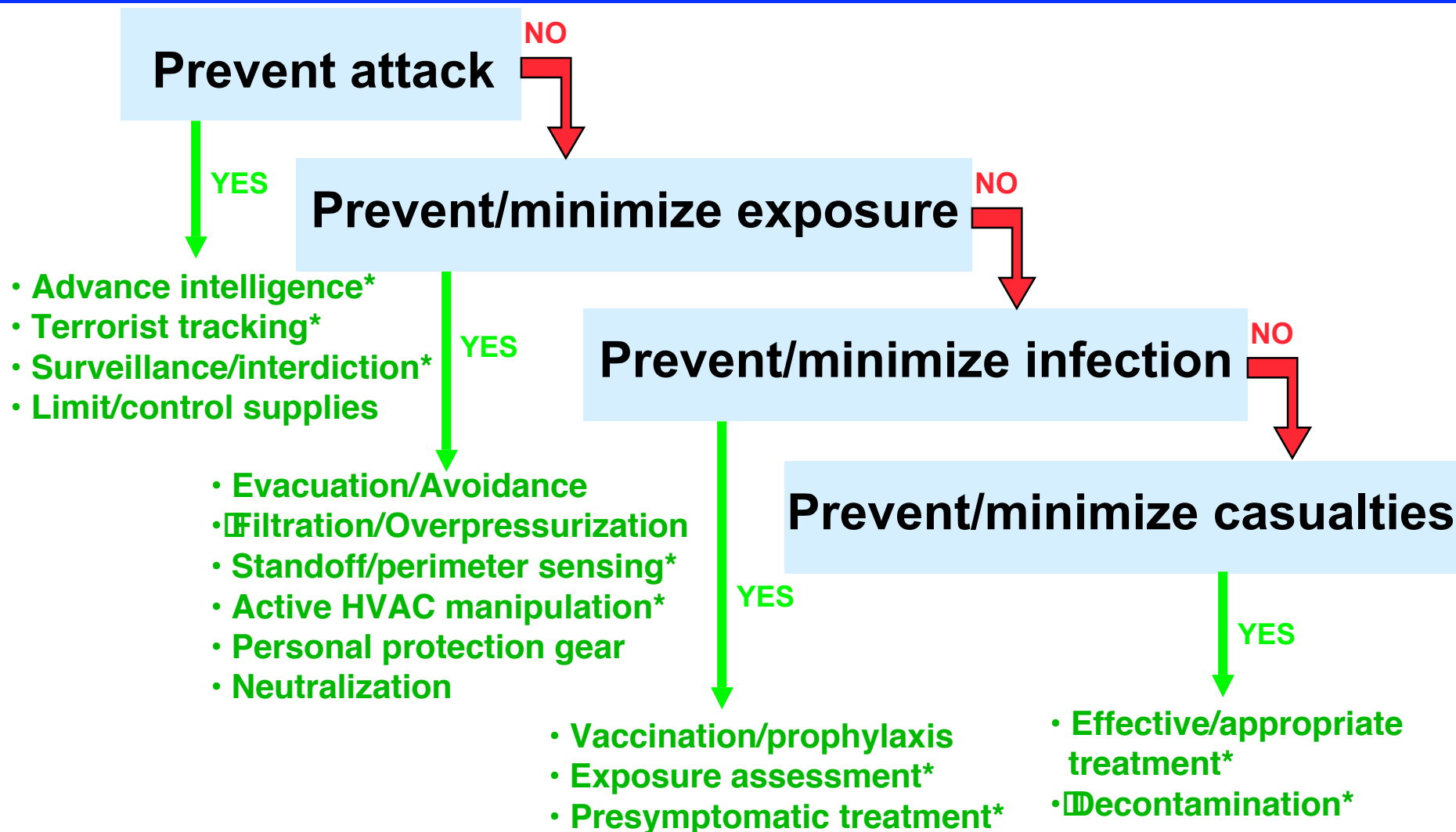
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Overall Biodefense Strategy



* Detection required

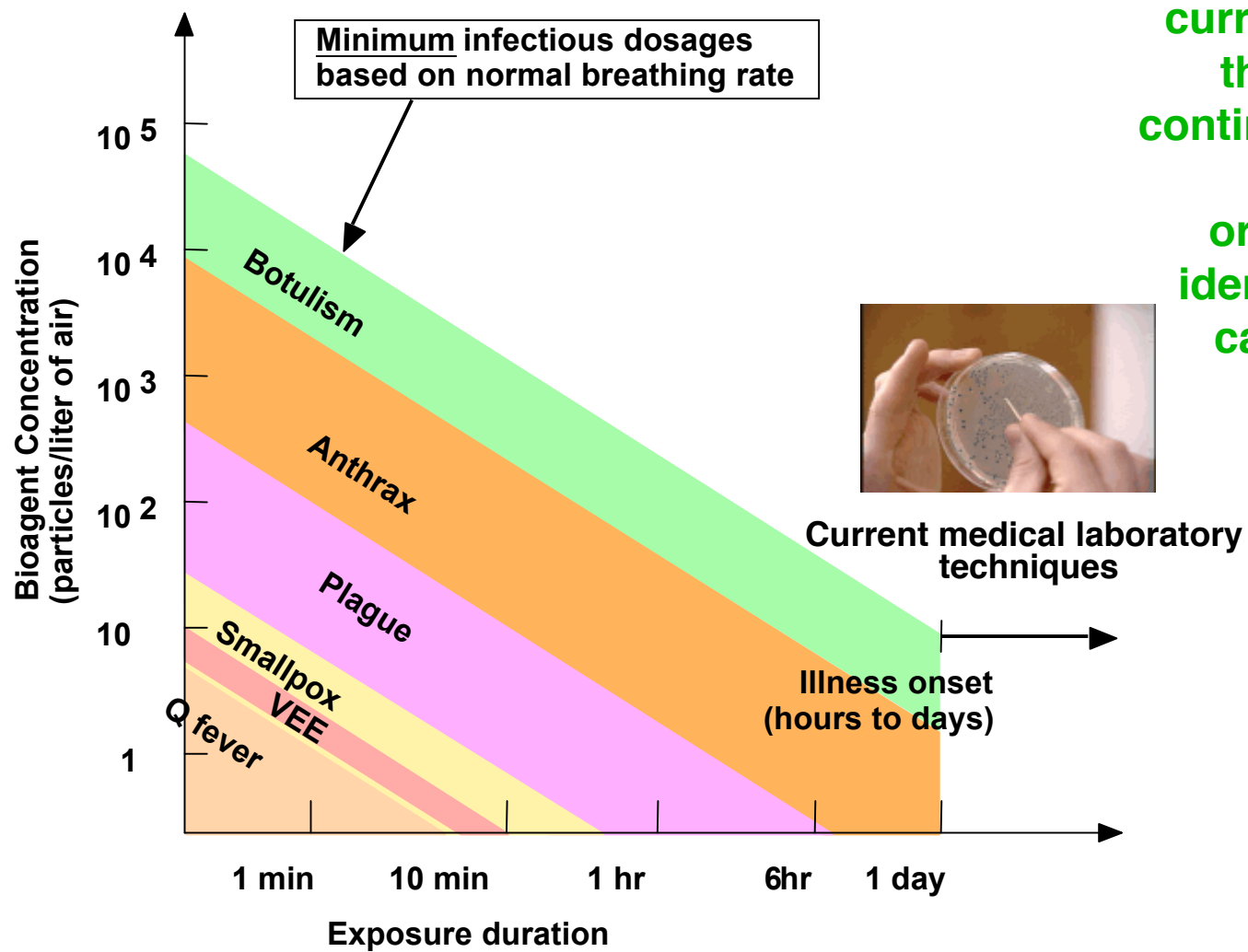


The Challenge of Biological Agent Detection

- **Protection requires rapid detection of pathogens in the environment (no false negatives, few false positives)**
- **Treatment and retaliation require accurate determination of the agent and its source**
- **Why is this so difficult?**
 - **Even low concentrations can be lethal**
 - **Aerosol are small (1 - 10 microns)**
 - Low scattering cross section
 - **Signatures can be non-specific**
 - Very different from chemical agents
 - **Biological technologies widespread that may mask signature**
 - **Competing backgrounds**
 - Natural and man-induced substances
 - Indigenous bioaerosol, including pathogens



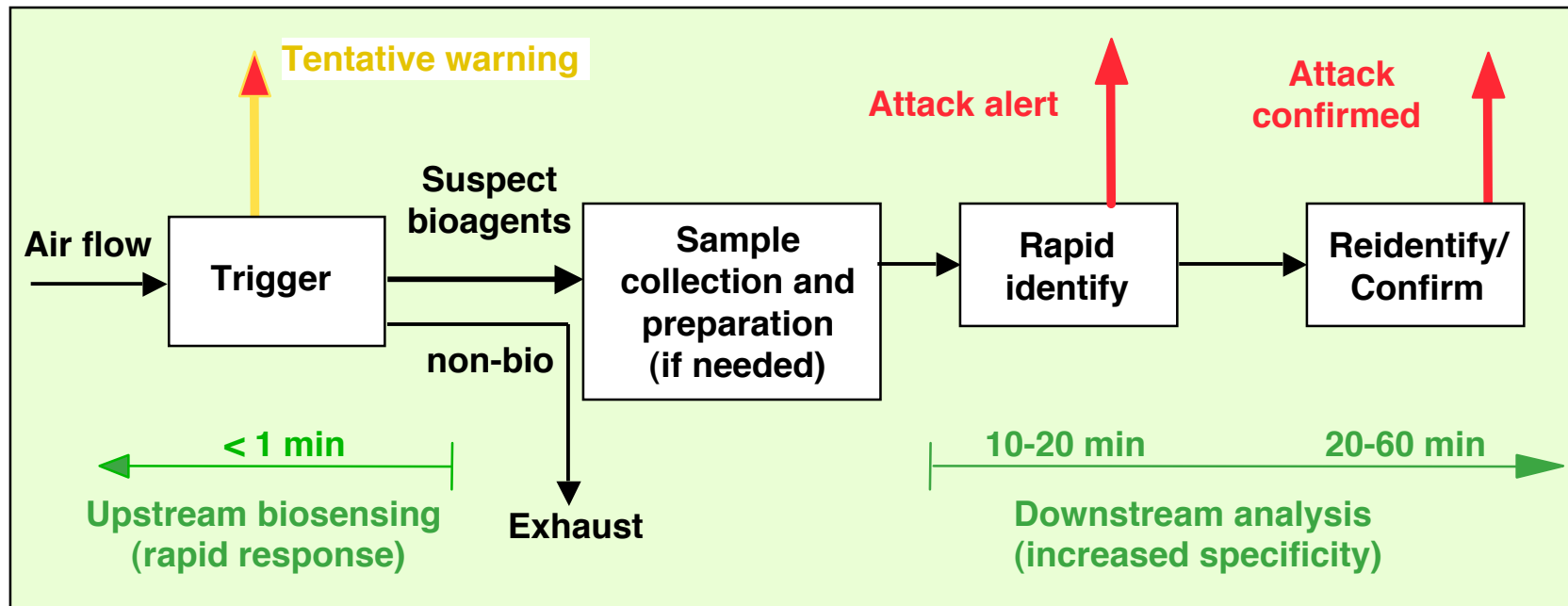
Sensing Requirements Driven by Understanding of Infectious Dosage



No sensing systems currently exist that offer continuous, real-time organism-identification capability



Generic Biosensor Architecture



- Particle count/sizing
- UV Laser-induced-fluorescence
 - Point
 - Standoff

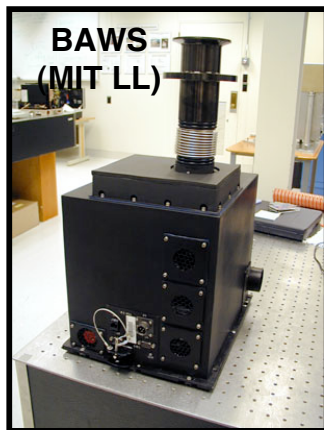
- Air-to-liquid collection
- Impaction
- Electrostatic separation

- Culture
- Immunoassay
- Cell-based
- PCR/DNA based
- Mass Spectrometry



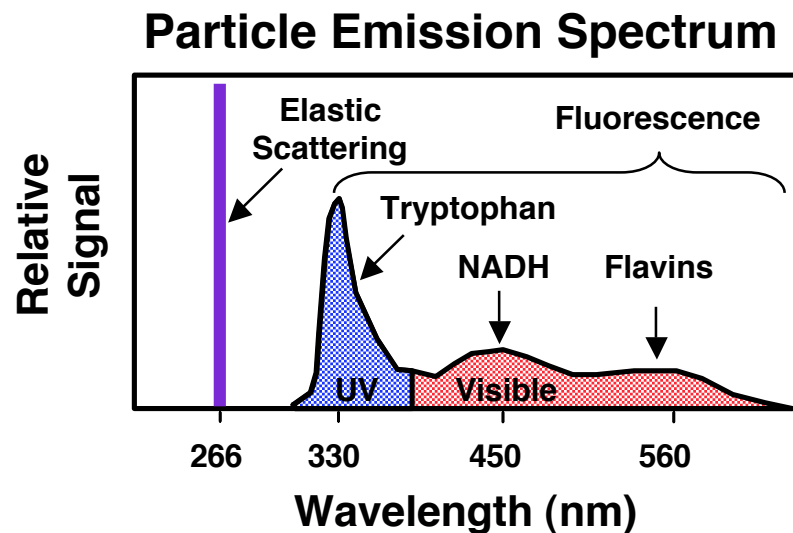
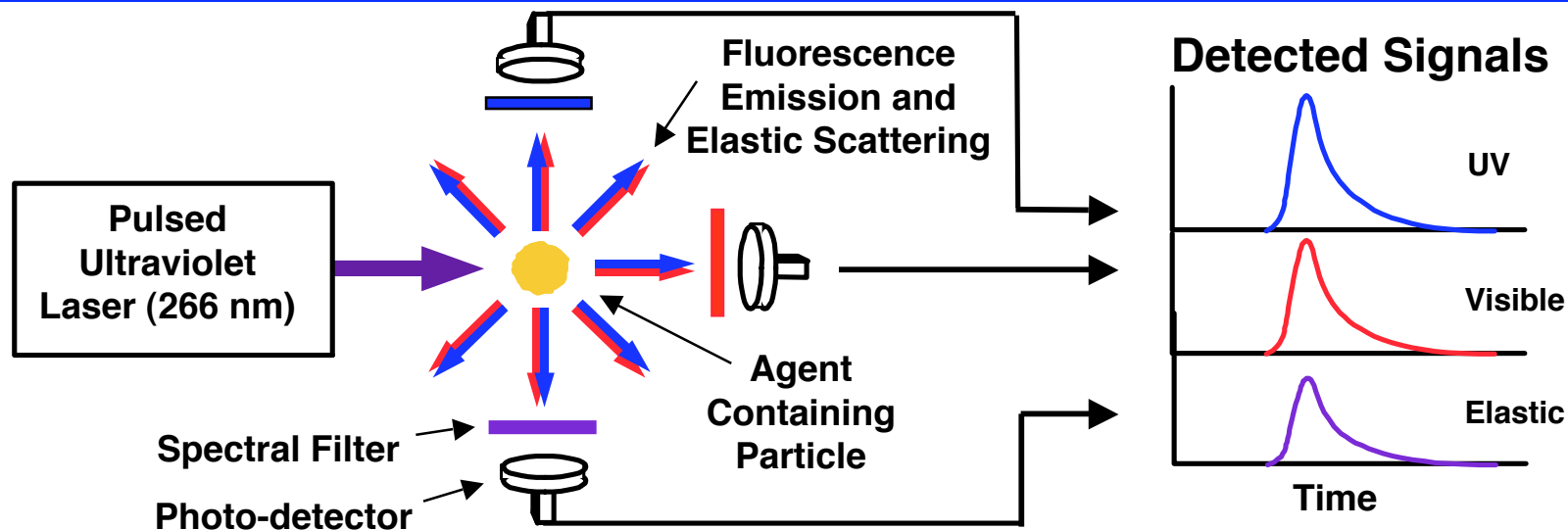
Examples of Trigger Sensing Technologies

- **Particle counting/sizing**
 - Simple, inexpensive, portable
 - Not specific to biologicals
- **UV Laser-Induced Fluorescence**
 - Offers biologic/nonbiologic differentiation
 - Has been developed for both point and standoff sensing

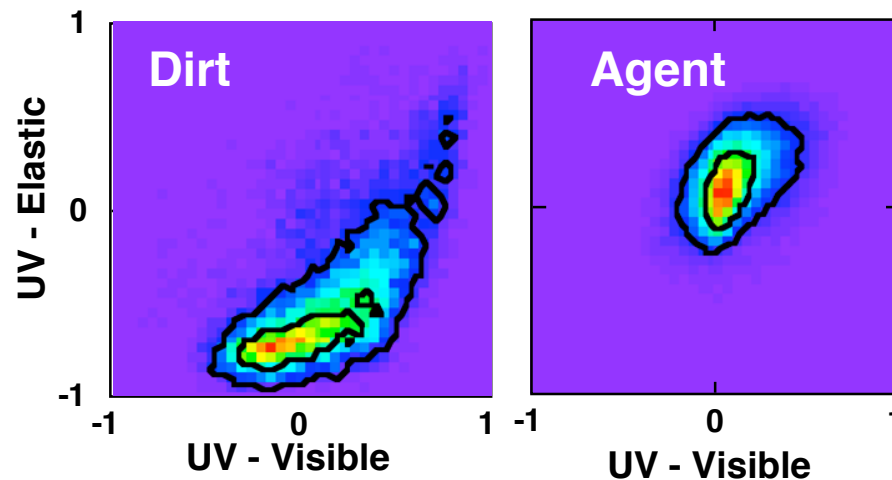




BAWS Principle of Operation



Particle Discrimination





Example of BAWS Response to Simulant Releases

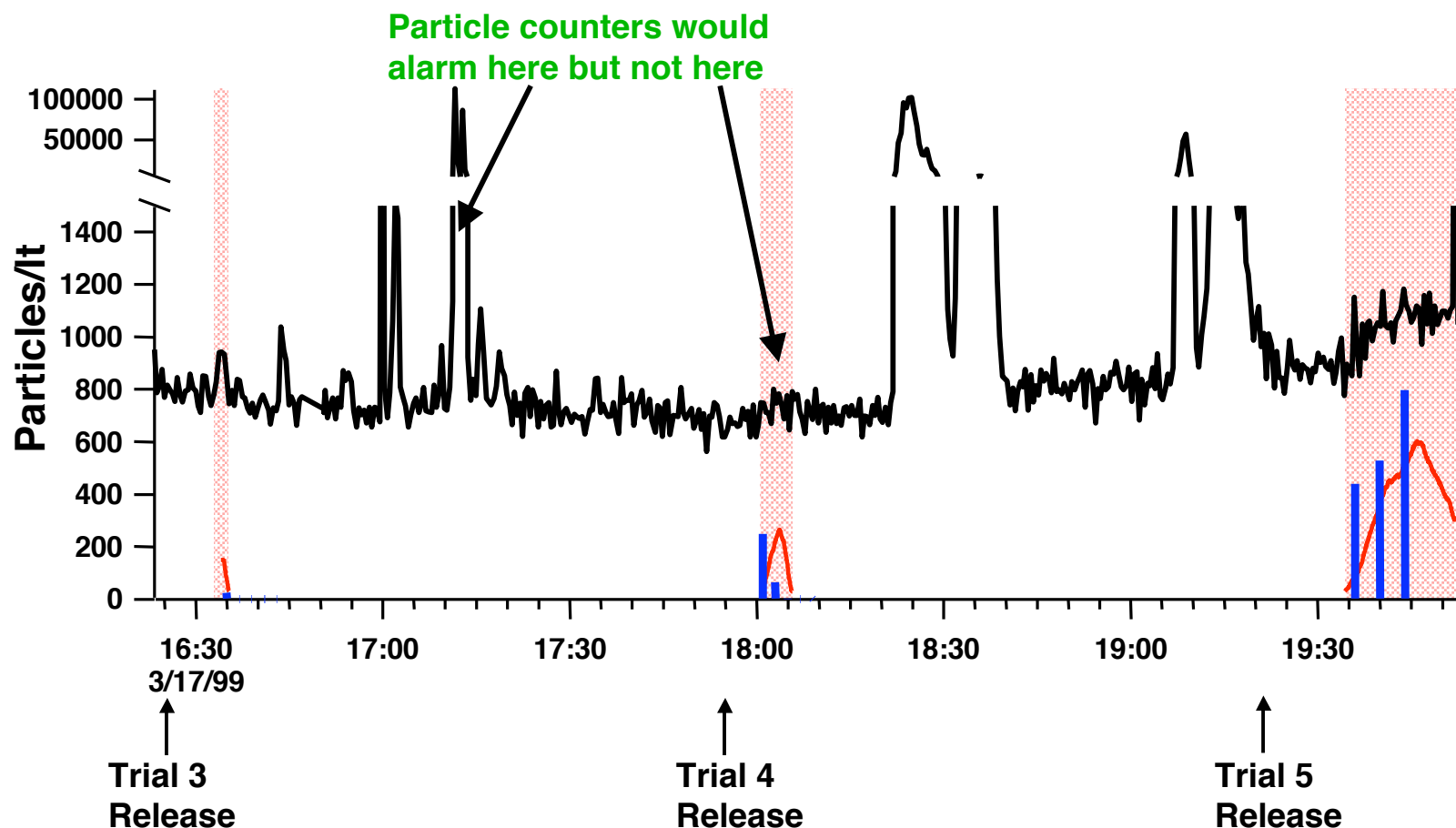
March 17, 1999
Dugway PreBLWE

Referee Data

- 2 - 10 μm particles (TSI APS)
- *Bacillus globigii* (STA sampler)

BAWS III Data

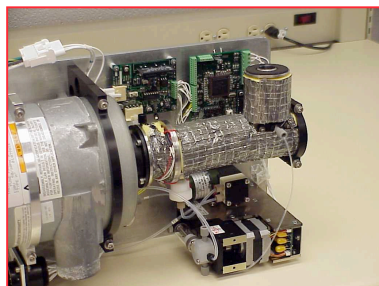
- Alarm window
- Agent





Collection of a Sample Following a Trigger

Air-Liquid Collection



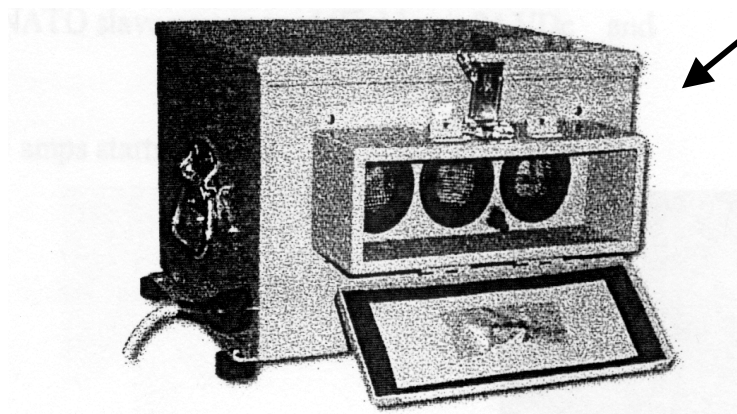
Wetted Wall Cyclone
(Battelle)



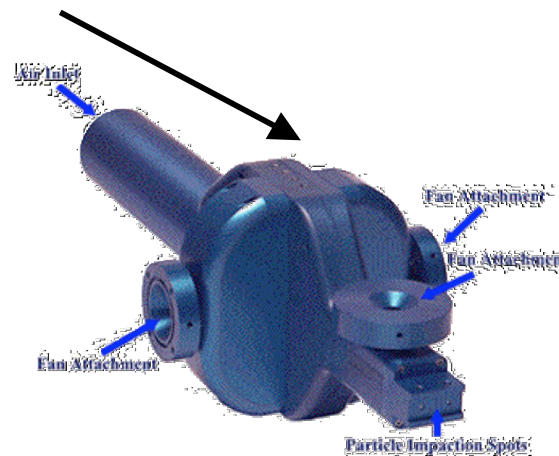
SpinCon (MRI)

- Collection systems can also be used for continuous monitoring
 - Periodic sampling and assay offers detect-to-treat for many threat agents

Dry Impaction



Dry Filter Unit



BioVic (MesoSystems)

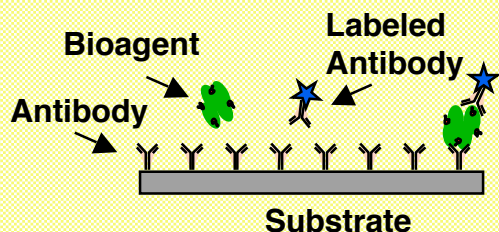


Current Bioagent- Identification Technologies

Response Time

Rapid ID

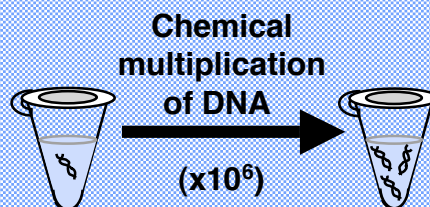
Immunoassays



- Selectivity from high affinity binding of antibody to agent-specific structures

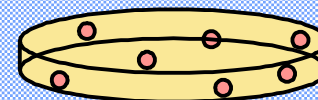
Orthogonal ID Confirmation Technologies

Polymerase Chain Reaction (PCR)



- Selectivity from sequence-specific DNA/RNA recognition
- Enzymatic amplification provides superb sensitivity

Culture-based assays



- Traditional method since Pasteur – still “gold standard” for ID
- Viable organisms replicated in culture and identified using biochemical assays and microscopy

Sensitivity/Accuracy



Examples of In-Use Rapid Identification Techniques



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**Ticket cartridges and reader
for lateral-flow immunoassay
in Joint Biological Point Detection System
(JBPDS)**



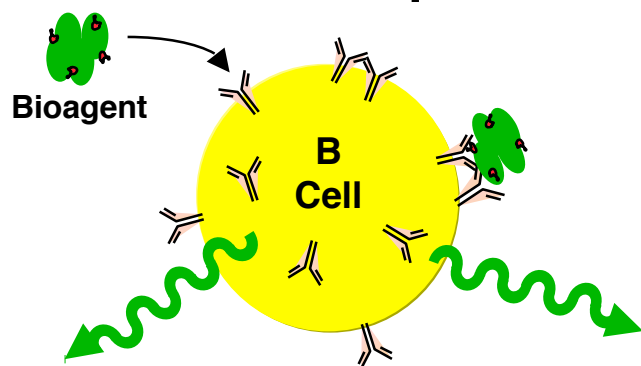
**Commercially available LFI tickets
and reader
(Tetracore/Alexeter)**

- Immunoassay-based tickets are relatively fast and require minimal sample preparation but their sensitivity is often poor and readout fairly subjective for low concentrations



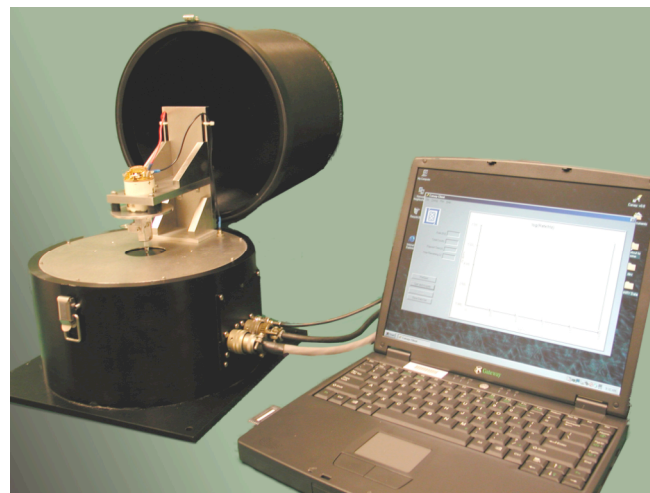
Developmental Bioagent-ID Sensor: CANARY (DARPA/MIT LL)

Concept



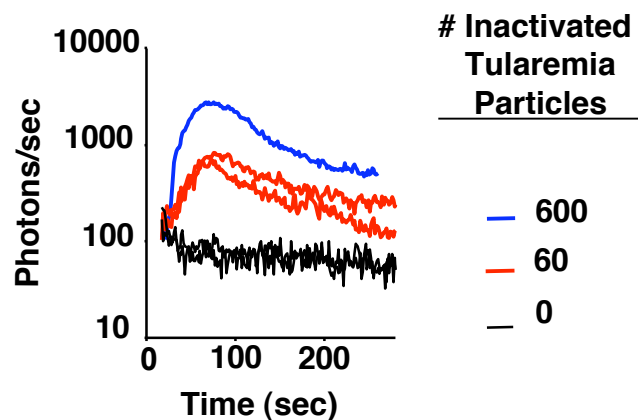
B cell emits ~200 photons within
30 seconds after bioagent binding

Prototype microcentrifuge device



Tests Against Killed Tularemia

(Collab. with NMRC)





Confirmation Identification Technology

- Systems being developed (and deployed) that provide agent ID within 30 minutes of introduction of prepared sample
- Challenge remains in automating sample preparation and analysis

Semi-automated field-portable
PCR devices



RAPID - Idaho Technologies



***SmartCycler
XC System - Cepheid***

Example of handheld PCR
device



Bioseeq - Smiths



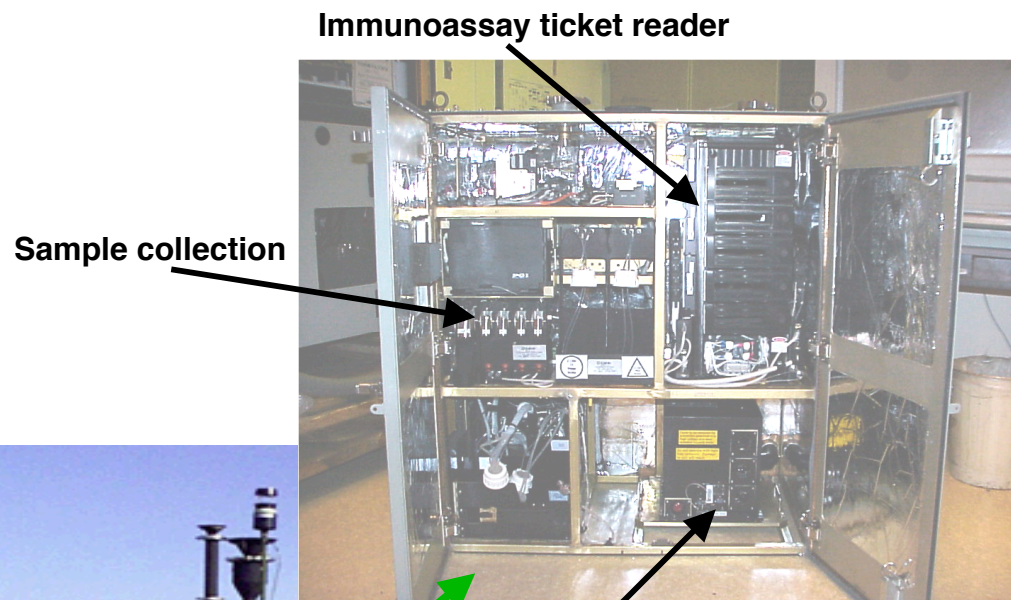
Examples of Integrated Systems



**Biological Integrated
Detection System (BIDS)**

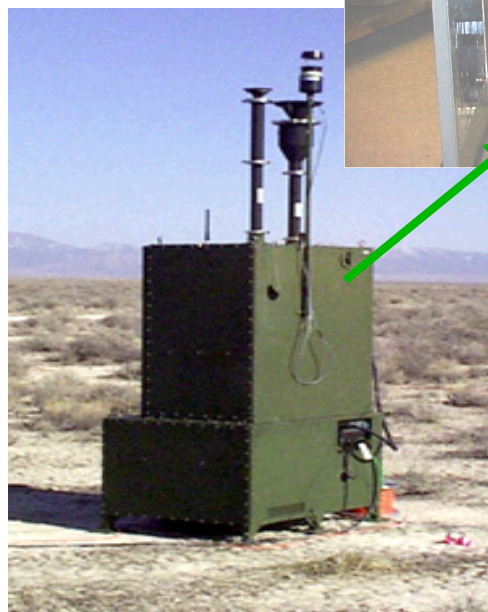


Portal Shield



Sample collection

Immunoassay ticket reader



**Joint Biological Point
Detection System (JBPDS)**

BAWS trigger



Military versus Civilian Detection Systems

- **Military systems developed primarily for outdoor force protection**
 - Emphasis has been on preserving functionality during assault (i.e., put masks on) and minimizing exposure (avoidance)
- **Technology limitations on real-time detection and identification have driven users to multi-stage architectures**
 - Fast non-specific trigger sensors followed by sample collection and multi-tiered assay
- **Civilian Biodefense can borrow from military investment but requirements do differ**
 - The most successful technologies will offer benefits above and beyond those given by Biowarfare protection (e.g., better infectious disease control, early diagnostics, exposure assessment, treatment, etc.)